discharging ears in the determination of raising quarantine in scarlet fever cases.

In conclusion, let me emphasize the importance of early recognition of the ear complications of scarlet fever; we should not expect and wait for the ear to "break and run," as is so often done, for this is but little short of criminal negligence, but, through prompt treatment by paracentesis of the tympanum as soon as there is the slightest indication of inflammation in the tympanic membrane or exudate in the tympanic cavity, relieve the distressing symptoms and place the patient in the safest possible condition as regards systemic infection and intracranial complications, and do all in our power to preserve the function of one of the most important organs of special sense.

CONCERNING THE CAUSES OF GALLSTONES.[1]

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My purpose in presenting this short paper to this Society is twofold. First, I wish to indicate a new method of investigating a very difficult problem, the causation of gallstones, and to show what results this new method of investigation has borne in my hands. Secondly, I want to interest the members of this Society, who are in a position to examine organs derived from a large number of autopsies, in this method of investigating, so that more cases may be brought together and studied, and the correctness of my data be either verified or denied.

Without going into the earlier history of the theories of gallstone production, which would lead us far astray and tend to obscure the points that I wish to emphasize, I would like to unfold to you the development of the present theory of gallstone production. This development is closely bound to the Strassburg school of medicine, to Naunyn and his pupils. The work of this school gave us our present conception of the etiology of gallstones.

Before the publication of these modern views the whole question of gallstone production was unsettled—just as unsettled as the questions of the etiology of pulmonary consumption prior to Koch's discovery. Diathesis, heredity, age, sex, were regularly named as the causes of cholelithiasis, while the actual processes at work were scarcely considered. In the early nineties Naunyn attacked these time-worn causes and he applied all his energies to the annihilation of the diathetic theory and to the building up of a new theory based on bacteriological facts. As was perfectly proper and logical, he set to work to determine the origin of the substances found in gallstones. Bile-pigments, cholesterin, and the organic framework had to be studied and investigated. He had to determine whence they came, under what conditions they were produced, and whether they were increased or diminished by changing the conditions of the experiments. In this work, Kausch, Thomas, and Jankau were of the greatest assistance. From the data furnished by these experimenters and investigators, Naunyn concluded that (1) the solids in bile are independent of general body conditions, that cholesterin is a product of the bile passages, and as such is not influenced by any diathetic or non-local conditions; that (2) bacteria enter the bile system, set up an inflammation, catarrhal in type, which blocks the free outflow of bile, and which is accompanied by an increased production of cholesterin, from the inflamed mucous membrane of the gall-bladder, and *pari passu* an exudation of albuminous substances. In this bacterial catarrh all the elements of the gallstones are present and by processes of precipitation and infiltration stones develop absolutely independently of the general body conditions.

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[1] Read before the New York Pathological Society, March, 1905. Since reading this paper I have been able to add a new case to my series.

When this view was published no convincing experiments were put forth to establish the positive fact that infection of the bile passages actually produced gallstones. That work was reserved for others and a number of years elapsed before this evidence was furnished. Mignot and Mijake succeeded in producing gallstones experimentally in animals by first partially occluding the cystic duct, thus producing incomplete stagnation of the bile, and then introducing bacteria into the gall-bladder and causing an inflammation of this organ. This work gave the firm support that Naunyn's theory had lacked when it was originally published. Since Mignot and Mijake did their work, others have repeated the experiments with varying results, but no one seems to have tried to follow and analyze the genesis of stones in the human body.

It seemed to me that if certain cases could be studied, I would be in a position to trace the development of gallstones in the human body. To obtain the same or similar conditions to those of the experiments of Mignot and Mijake, I would have to get livers in which there was stagnation of bile and infection of the biliary ducts, as the gall-bladder in acute inflammatory conditions rarely comes to the post-mortem room unopened. Patients are either operated and the bladder is emptied or they get over the acute attack and we know not what has occurred in the bladder. The few that die of this condition represent the most acute cases, and, as they are of short duration only, the study of stone formation is practically impossible because of the early stage of development of the same. These facts turned my attention to the liver and its ducts. Here we find obstruction and inflammatory conditions combined; here in cases of common duct obstruction and secondary cholangitis the conditions obtained by the animal experiments are paralleled. In these cases, which unfortunately for this investigation are rather rare, nature reproduces the conditions that Naunyn thought underlay the process of gallstone production. The conditions are purely local; there is stagnation of bile and there is inflammation of the mucous membrane of the bile passages. If it were possible to obtain a sufficiently large number of human livers with the above conditions present, the correctness of Naunyn's views, as well as the direct applicability of the results of animal experimentation, might be verified and the theory of gallstone production in human beings would rest on a firm basis.

I was able to collect 12 cases at autopsy[1] in which there had been a common-duct obstruction for more than four or five weeks, and in which a more or less severe inflammation of the extra and intrahepatic ducts had developed. In 7 of my cases the common duct was obstructed by calculi, in 5 by tumors of various kinds. *In the first series of 7 cases, as a result of the conditions of the experiments stones formed in the liver-ducts. In the second series of 5 cases, though apparently the same conditions were present, no stones developed, though stagnation of bile and inflammation of the mucous membrane of the bile passages were present.* In this second series Naunyn's causes were present just as in the first series, but no stones developed. How are we to explain this difference? Why should gallstones be produced in the liver-ducts in one series and not in the other? Is it mere chance that cases with previous cholelithiasis regularly showed stone formation in the liver-ducts, when common-duct obstruction due to stone and cholangitis developed, while those that had no previous stone formation did not develop stones, when stagnation of bile and cholangitis developed?

The absolute regularity in the results seems to me to preclude chance, and even though my series of cases be small, I think it points to a new factor in the production of gallstones. It is needless to theorize at this stage as to what this factor may be. If, to make my point clearer, we call the third factor an altered liver metabolism or a diathesis, we could understand why stones developed in the liver-ducts when stagnation and infection developed in cholelithiasis cases (they having the predisposition as evidenced by the older stones), and why they would not develop under similar conditions (second series) where no liver disturbance or diathesis obtained. But the term diathesis is vague and almost meaningless, merely a garb for ignorance. Perhaps, however, a faulty hepatic metabolism underlies the formation of gallstones?

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[1] Similar cases of the clinical surgical literature have been brought together by me in a paper entitled "Intrahepatic Cholelithiasis," Medical News, 1904.

A larger material bearing on this subject could readily be gathered by the members of this Society without entailing any great trouble, and a larger material would help to clear up this difference that I have described between the cases of old cholelithiasis and those without cholelithiasis. And, as I said at the outset, it was with the purpose of enlisting your assistance that I read this paper.

In closing I may sum up the results that I have obtained as follows:

1. *Naunyn's factors—stagnation of bile plus inflammation of the bile-passage mucosa—do not seem to be sufficient by themselves to lead to gallstone formation, even though the time allowed for the working of the causes be adequate.*
2. *My first series of cases shows that these two factors lead to stone formation in patients who previously had gallstones. In this series we have the first real evidence of the factors underlying gallstone production and the causes of cholelithiasis in human beings.*

A CONTRIBUTION TO THE DOCTRINE OF THE MORPHOLOGY OF THE BLOOD, DERIVED FROM EXPERIMENTAL TOLUYLENDIAMINE POISONING.[1]

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The advances made in staining methods in recent years have increased the range and certainty of our classification of changes in the morphological elements of the blood. This was notably the case after the application of Ehrlich's method, a fact which may have led that author to state so optimistically that the doctrine of the changes in the blood, in as far as it depends upon morphological investigations, especially with the aid of color analysis, belongs to the, for the greater part, enlightened chapter of general pathology, and appears to have reached, provisionally, a definite conclusion, so that, essentially, only a few points remain to be cleared up.

Against this encouraging view is the constantly increasing list of contemporary works dealing with the blood morphology from clinical, pathological, and anatomical standpoints. As example, one

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[1] Based upon a series of experiments conducted under Dr. Julius Arnold at the Pathological Laboratory of Heidelberg in 1901.

Schluss-betrachtung zu der Leukaemia, Bd. viii. der spec. Pathologie u. Therapie, Wien, 1901.